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From: Baskar, Padmavathi
Sent: Monday, June 30, 2003 8:17 AM
To: STIC-ILL
Subject: FW: 0930012PLEASE SEND THIS

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From: Baskar, Padmavathi
Sent: Monday, June 30, 2003 8:14 AM
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Subject:

PLEASE PROVIDE THE FOLLOWING, i DID REQUEST THIS UNDER QP6.31.T69 BUT DID NOT RECEIVE THIS. I APPRECIATE IF U COULD SEND ME THIS.

VENOM RESEARCH AT TEXAS A&M
HIGH TECH SEPARATIONS NEWS 1996, V9,N4, SEP1 1996

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HIGH TECH SEPARATIONS NEWS

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In This Issue...

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NOVEL METHODS

IBC Bonding with Millipore

Researchers at IBC Advanced Technologies, Inc. (856 E. Utah Valley Dr., American Fork, UT 84003; Tel: 801/375-1600, Fax: 801/763-8491) and Millipore Corp. (80 Ashby Rd., Bedford, MA 01730; Tel: 617/275-9200, Fax: 617/275-5550) have joined forces to develop a method for removing, separating and concentrating certain selected ions from a mixed solution using ion-binding ligands bound to membranes (U.S. Patent 5,547,760).

The compositions described comprise ion-binding ligands that are covalently bonded to a membrane through an amide, ester, thioester, carbonyl or other suitable bond. Membranes that are inherently hydrophilic, or partially hydrophilic, and contain moieties appropriate for making these bonds are preferred. Such membranes include polyamides, such as nylon, and cellulosic materials, such as cellulose, regenerated cellulose, cellulose acetate, and nitrocellulose.

If the membrane used does not contain reactive groups it can be modified or derivatized. A composite membrane made up of a porous polymer membrane substrate and a deposited insoluble, cross-linked coating might also be useful.

Representative suitable polymers forming the membrane substrate include fluorinated polymers such as poly(tetrafluoroethylene), polyvinylidene fluoride, and the polyolefins such as polyethylene, ultrahigh molecular weight polyethylene, polypropylene, or polymethylpentene. Other possibilities include polystyrene, polysulfones, polyethersulfone, polyesters, polyacrylates and polycarbonates. Copolymers can also be used for forming the polymer membrane substrate, such as copolymers of butadiene and styrene, fluorinated ethylene-propylene copolymer, ethylenechlorotrifluoroethylene copolymer.

The ligand portion of the composition forms a complex with the selected ions and removes them from the source solution. The selected ions are then removed from the composition through contact with a much smaller volume of a receiving solution in which the selected ions are either soluble or which have greater affinity for the selected ions than does the ligand portion of the composition. This serves to quantitatively strip the complexed ions from the ligand and recover them in concentrated form in the receiving solution.

The process is useful in the re-

moval of selected ions, including noble metals and other transition metals from a variety of source solutions such as are encountered in semiconductor, nuclear waste cleanup, metals refining, environmental cleanup, providing ultra high purity fluids, electric power, and other industrial enterprises.

Drug Discovery Speeds Up

Selectronics, a proprietary drug discovery technology developed by PerSeptive Biosystems (500 Old Connecticut Path, Framingham, MA 01701; Tel: 508/383-7700, Fax: 508/383-7880), integrates computerized automation with advanced biochemical separation and detection techniques. The method addresses a key rate limiting step in drug discovery, namely converting chemical diversity into drug leads.

Selectronics combines multi-step chromatography, affinity selection, and mass spectrometry to achieve a very high throughput selection of new drug lead compounds from a variety of chemical sources including chemical combinatorial libraries, natural product libraries, and synthetic chemical files.

The technique involves the use of an affinity target as a "bait on a hook" to "fish-out" from among a complex mixture, typically containing tens to millions of chemicals, compounds with tight-binding affinity toward the target. Using multi-step chromatography with mass spectrometry identifies the selected lead compound(s) in a single pass.

Multi-step chromatography is used to prescreen and, after selection, further separate the chosen compounds without manual handling at very high speeds. The output is then fed to a mass spectrometer where compounds are identified by mass alone or by their characteristic fragmentation pattern. Selectronics relies on advanced proprietary mass spectrometers which combine high sensitivity, resolution, and mass accuracy.

The technology is highly flexible and can accommodate single or multiple targets simultaneously and can isolate binders with affinities ranging from nanomolar to micromolar. Using the Selectronics technology, PerSeptive claims that active compounds can be selected from complex libraries in time frames of hours to a few days.

GEL/SLAB ELECTROPHORESIS

PEG-Induced Pore Size Heterogeneity

Derivatization and molecular weight reduction of the agarose gel have been used to increase pore size heterogeneity. As an alternative to these methods, Philip Serwer and a University of Texas Health Science Center (Dept. of Biochemistry, San Antonio, TX 78284-7760; Tel: 210/567-3765, Fax: 210/567-6595, email: Serwer@uthscsa.edu) research team have been testing excluded volume, as a means of inducing pore size heterogeneity in agarose gels.

The team's results indicate that adding polyethylene glycol (PEG) of high molecular weight (18,500) to molten agarose before gelation increases pore size heterogeneity in gel electrophoresis. Conversely, Serwer et al. have found that adding a PEG with a lower molecular weight (4,000 or 7,500) results in micron-sized precipitates forming in a gelled network of agarose fibers. In an article in *Electrophoresis* [17, 971-976, 1996], the team writes that the PEG-induced heterogeneity of pore size occurs primarily in the 100-1,000 micron scale zones. These zones are separated from each other by interzone regions of decreased agarose fiber density.

An increase in excluded volume results from either the increased intermolecular binding or the increased unimolecular condensation that results from adding the PEG. The excluded volume drives the segregation of agarose during the increased turbidity during gelation with PEG. The authors doubt that the amount of excluded volume controls the type of segregation that occurs.

Despite their success in PEG-induced pore size heterogeneity, the Serwer research team has determined that more uniform gels are needed for the study of sieving. The scientists are now working on formation of a more continuous gel.

Contour Clamp Controls the Field

Gel electrophoresis is capable of separating macromolecules (i.e., proteins and nucleic acids) on the basis of size, charge, and/or conformation. Most applications involve the use of a single pair of electrodes to generate the electric field. Such a field is necessarily constrained to be uniform and oriented in a single direction, and as a result conventional techniques are limited in many respects.

A gel electrophoresis device developed by Gilbert Chu, Douglas Vollrath, and Ron Davis of

Stanford University (Dept. of Medicine-Oncology, Work Location M213, Stanford, CA 94305; Tel: 415/725-6442) arranges a number of electrodes around a closed contour that offers certain advantages over conventional techniques. The contour clamping controls the migration of particles by manipulating the shape and orientation of the electric field in the gel.

The use of contour clamping enables the high resolution separation of macromolecules (particularly DNA molecules up to or greater than 2 megabases in size), by gel electrophoresis whereby the pattern of separation is independent of position in the gel. The newly discovered technique provides a means for separating relatively small macromolecules (such as DNA of less than 50 kilobases), without distortion even at high voltage. It also provides a means of identifying secondary structures in macromolecules and minimizes band broadening in the electrophoretic separation of macromolecules.

Chu et al. predicated their invention in part on the discovery that the limitations inherent in the existing electrophoretic separation techniques can be overcome by applying contour-clamped uniform or nonuniform electric fields. They define the term "contour-clamped electric field" as an electric field that is generated by multiple electrodes arranged along a closed contour clamped to predetermined electric potentials. The term "uniform electric field" they say means an electric field having a uniform direction and magnitude within a closed contour.

Depending upon the particular application for the method and device, Chu and his research team subject the gel to a uniform or nonuniform field by clamping a number of electrodes at predetermined potentials. Where at least two electrodes are clamped to different potentials, they serve as the driving electrodes. Where at least two more electrodes are clamped to intermediate potentials, they serve to further define the nature of the electrical field.

In U.S. Patent 5,549,796, Chu et al. describe how two or more electrodes (the driving electrodes) are clamped at a potential difference phi_0 to establish the general orientation and strength of the electric field. The remaining electrodes are clamped to intermediate potentials that control the shape of the field established by the driving electrodes. Chu and his researchers vary the electric field, in accordance with the purpose of the electrophoresis. The amount of variation depends upon the size of the particles and the information to be determined concerning the particles.

CAPILLARY ELECTROPHORESIS

Vancomycin Serves as Chiral Selector

Researchers at the Instituto di Chromatografia del Consiglio Nazionale delle Richerche (Area della Ricera di Roma, Box 10, 00016 Monterotondo Scalo, Roma, Italy) are using vancomycin as the chiral selector in capillary electrophoresis for the separation of enantiomers of loxiglumide. The separation of optical isomers represents an important field of application in analytical chemistry, particularly in pharmaceuticals. Salvatore Fanali and Claudia Desiderio report that loxiglumide, or D,L-4(4,4-dichlorobenzoylamine)-5-oxopentanoic acid, is a chiral drug administered in the pure D-enantiomer form for gastrointestinal pathology related to physiological levels of cholecistokinine disregulation.

The chiral separation was undertaken in an uncoated capillary at a pH of 6 in the presence of the electroosmotic flow. The presence of the vancomycin buffer in the path length of the detector strongly reduced the sensitivity of the capillary electrophoresis method. Improvements in both sensitivity and analysis time were obtained using a coated capillary where the very low electroosmotic flow allowed the use of the partial separation zone technique, making the detector free of vancomycin.

The enantiomeric resolution of loxiglumide was influenced by the vancomycin concentration and pH. The optimum experimental conditions were found using phosphate buffer at a pH of 6. Vancomycin dissolved in the running buffer present in part of the capillary. The optimized method was applied for the analysis of D- and L-loxiglumide in different preparations said to contain only the D-isomer. L-loxiglumide was not detected. The work is fully outlined in the *Journal of High Resolution Chromatography* [19, 322-326].

Designer Drugs Are Separated/Identified

Designer drugs, or synthetic addictive compounds, are all too easily synthesized in illicit laboratories. Capillary zone electrophoresis (CZE) has been used in recent years to separate methylenedioxyamphetamine-related designer drugs. To iden-

tify and separate these drugs, Zeynep Z. Gogus (Institut fur Pharmazeutische Chemie, Auf der Morgenstelle 8, 72076 Tubingen, Germany) and his colleagues developed an online capillary zone electrophoresis-ionspray mass spectrometry system.

The objective of the research was to find an unambiguous means of identifying this class of drugs in dilute samples (e.g., urine), without the necessity of pretreatment or concentration. In the *Journal of Chromatography A* [735, 221-226, 1996], the developers conclude that their CZE-MS methodology offers a fast and reliable means of identifying this class of designer drugs in the femtomole range.

To reach this conclusion, Gogus *et al.* coupled a Model 100 capillary electrophoresis system from Grom (Herrenberg, Germany) with an APIII quadrupole mass spectrometer from Sciex (Toronto, Canada) via ionspray interface. They prepared the following three buffer solutions: A - 40 mM sodium formate-10 mM sodium chloride (pH 2.5); B - 40 mM ammonium acetate-0.5 mM cetyltrimethyl-ammonium chloride (pH 5.5); and C - 50 mM sodium phosphate-10 mM ß-cyclodextrin (ß-CD)-5 mM triethylamine (pH 2.0). For CZE separations, the team chose fused-silica capillaries (50 micron I.D. and 375 micron O.D.) with a polyimide cladding from Polymicro Technology (Phoenix, AZ). For CZE-MS coupling, the researchers used capillaries of 50 micron I.D. and 180 microns O.D. They burnt off a 5 mm length of the polyimide cladding with a glowing wire to allow online UV detection.

Gogus *et al.* were able to separate the designer drugs with two of the three buffer systems used. Adding ß-CD to the buffer systems enabled the researchers to achieve chiral separations.

High-Sensitivity Diode-Array Detection

The diode-array detection incorporated into Hewlett-Packard Co.'s (HP Analytical Direct, 2850 Centerville Rd., Wilmington, DE 19808-1610; Tel: 800/227-9770) HP ^{3D}Capillary Electrophoresis system is specially designed for on-capillary detection. The system offers quantitative and qualitative analysis with excellent sensitivity, wide linear detection range, and full spectral capabilities.

Sensitivity is further enhanced by HP Extended Light Path capillaries. These capillaries contain a three-times expanded diameter section (bubble) at the point of detection. This design improves sensitivity up to a factor of three over standard (straight) capillaries, without sacrificing resolution.

The detector optics of the HP ^{3D}Capillary Electrophoresis system have been designed for a wide linear detection range by minimizing stray light. The use of HP Extended Light Path capillaries also improve the linear detection range. The signal is tripled by the length of the light path, and noise is decreased due to higher light throughput.

Compound identification and/or confirmation, peak purity checking, and easier method development are just a few of the benefits of diode-array detection. Data can be acquired at all wavelengths simultaneously, from 190 to 600 nm, without loss of sensitivity. Data can be displayed as isoabsorbance plots or as single-wavelength electrophoresis. The peak purity algorithm of the diode-array system reduces method development time, by determining the purity of non-Gaussian peaks.

The diode-array detector is one of the functional parts for CE separation contained within the HP ^{3D}Capillary Electrophoresis instrument. The instrument is one of the components of the fully automated HP ^{3D}Capillary Electrophoresis system. Other components include the HP ^{3D}CE Chemstation, HP Extended Light Capillaries, and accessories. The system provides the flexibility needed for advanced method development and the standardized protocols required for routine operation.

The HP ^{3D}Capillary Electrophoresis system is equipped with a single sample carousel that allows random access to all vials for autosampling and fraction collection. Vials are fully-sealed and the carousel is thermostatically-controlled to prevent sample evaporation and degradation. Valuable positions in the sample carousel are not required for multiple buffer vials. Buffer pH values and composition are kept stable during analysis of multiple samples by an off-line buffer replenishment unit. The unit can empty and refill vials with fresh buffer during analysis. Vials can be filled to a user-determined level to avoid siphoning of buffer during analysis.

Injection of nanoliter quantities is a delicate task and is critically important for quantitative reproducibility. The HP ^{3D}Capillary Electrophoresis system uses self-correcting pressure injection to improve quantitative analysis. The system constantly measures injection pressure, compares it with the programmed value, and, if necessary, corrects it. Reproducible electrokinetic injection is also available for use with gel-filled capillaries or other applications.

Capillary temperature control is important for reproducible migration time and accurate quantitative analysis. The HP ^{3D}Capillary System offers efficient heat re-

moval and controls capillary temperature from 10°C below ambient up to 60°C. To ensure low running costs and ease of use, the system uses recirculating, high-velocity air flow with Peltier temperature control. The temperature control system is self-correcting for changes in ambient temperature.

Watching ver Wine

In 1992, the University of California at Davis established the feasibility of using capillary electrophoresis for wine analysis, and now, for the first time, CE is being used routinely to analyze the chemical composition of wine.

Using a BioFocus CE system from BioRad Labs (2000 Alfred Nobel Dr., Hercules, CA 94547; Tel: 800/4BIORAD or 510/741-1000, Fax: 510/741-1060), CE was shown to be a reliable method for determination of free sulfur dioxide in wines. Later, methods for analysis of organic acids and sugars were developed. In the fall of 1994, BioRad collaborated with UC Davis in a field evaluation of CE methods at the Trefethen Winery in Napa Valley. The success of this evaluation caught the attention of vintners and wine analysis labs throughout the state. Two major wineries purchased BioFocus systems for use in the harvest.

The two major applications for CE in wine analysis are monitoring malolactic fermentations and determination of residual sugar. Determination of malic and lactic acids is very easy to perform by CE, and acetic acid, an undesirable product of another bacterial fermentation, can be detected in the same separation. Conventional methods for determination of residual sugar employ expensive enzymatic tests, while sugar analysis by CE is rapid and inexpensive. In the 1995 harvest, organic acid and sugar levels were determined on literally thousands of samples using the BioFocus system. In one case, the quick results provided by the CE analysis allowed the vintner to detect a problem fermentation early and save thousands of gallons of product from spoilage. The cost savings provided by increased sample throughput and reduced labor costs enable an instrument payback schedule of 24 months.

Additional CE analyses are being developed for ethanol, sorbate, inorganic ions, and amino acids. The flexibility and simplicity of capillary electrophoresis promise to make it a routine analytical technique throughout the wine industry as well as in other segments of the food and beverage industry.

Chiral Resolution with b-Cyclodextrin

Scientists at Peking University (College of Chemistry and Molecular Engineering, Beijing 100781, China) and Beijing Institute of Technology (Dept. of Chemical Engineering and Material Sciences, Beijing 100081, China) used capillary electrophoresis with b-cyclodextrin to separate diastereomers of 1,2-disubstituted tetrahydro-b-carboline. Li Zhang, of Peking University, reports that 3-acetyl-1,4,6,7,12,12*b*-hexahydroindolo[2,3-*a*]quinolizine is an important building block in the synthesis of various indole and oxindole alkaloids.

The key reaction in the 9-step enantioselective synthesis of this compound from l-tryptophan is the asymmetric condensation of L-tryptophan methyl ester to yield diastereomers of methyl 1-(2,2-dimethoxyethyl)-1,2,3,4-tetrahydrocarboline-3-carboxylate.

A possible mechanism explaining the chiral separation, report the Chinese researchers, involves the structural features of the analytes and the type of cyclodextrin. It is possible that if no inclusion complex is formed, the diastereomers cannot be resolved from one another in aqueous solution. The mechanism is believed to be the formation of an inclusion complex between the analyte and the b-cyclodextrin. First, the diastereomers have a hydrophobic indole ring structure which fits into the cavity of b-cyclodextrin. Second, the hydroxyl groups on the rim of the b-cyclodextrin interact with the methoxy groups near the stereogenic center of the analyte by forming hydrogen bonds.

The interaction is stronger for one isomer than for the other and the resolution can be accomplished. The scientists, published their work in *Chromatographia* [**42**(7/8), 385-388]. They suggest that additional investigations would be helpful, including binding studies involving the analyte and the b-cyclodextrin.

CHROMATOGRAPHY

Light Scattering Detect r Debuts

Polymer Labs, Ltd. (Essex Rd., Church Stretton, Shropshire SY6 6AX, England; Tel: +44/1694 723581, Fax: +44/194 722171) commercialized its PL-EMD 960 evaporative light scattering de-

tector for high performance liquid chromatography (HPLC), gel permeation chromatography (GPC), and high temperature GPC (HTGPC) applications. Laura Watson, marketing manager, says that the new device has advantages over other concentration detection systems by allowing the detection of samples without ultraviolet (UV) chromophores or when using UV opaque eluents, and for gradient HPLC without drifting baselines or "solvent" effects. The PL-EMD 960 instrument is said to be the ideal replacement for a refractive index detector for most applications and uses in which rapid start up and equilibrium, or steady baselines are required.

Design improvements in the PL-EMD -960 ensure increased sensitivity and reduced gas consumption. Improved nebulization allows lower temperature operation, which, together with overall noise reduction, provides for a significant increase in detection levels across a wide range of HPLC applications. To provide maximum applications capability, the PL-EMD 960 permits the widest operating temperature of any evaporative light scattering detector—ambient to 200°C—and is said to be the only system to support elevated and high temperature GPC, through the use of a detector controlled heated transfer line. The company's U.S. operation, Polymer Labs, Inc. is located at Amherst Fields Research Park, 160 Farm Rd., Amherst, MA 01002; Tel: 413/253-9554, Fax: 413/253-2476.

High pH Bonded Phase Packing

Low pH levels are often recommended for the reverse phase separation of basic compounds, because these pH levels produce the best peak shapes and highest column efficiencies. Chromatography at low pH is sometimes not feasible because of solute instability or band spacing problems. In such cases, an intermediate pH range (4-8) or a pH of greater than 9 is often used.

Although intermediate pH operations can produce useful band spacings for ionizable compounds, problems with band shapes and retention reproducibility can arise as a result of the partial ionization of the basic solutes, the unreacted silanols, or a combination of both on the silica support surface. Operation at higher pH, at least 9, is potentially attractive because basic compounds can be separated as free bases. This minimizes interaction with the silica support. In this case, silanol groups on the support surface are ionized so that electrostatic interaction with free base solutes cannot occur.

Separations with silica-based columns have traditionally been discouraged because of possible problems with silica support dissolution and rapid column failure. Researchers at Rockland Technologies, Inc. (538 First State Blvd., Newport, DE 19804; Tel: 302/633-5880) have found that certain densely bonded, non-endcapped dimethyl-C_{18} bonded phase high performance liquid chromatography (HPLC) packings prepared with sol-gel porous silica microspheres are surprisingly resistant to degradation in the pH 10-12 range. Jack Kirkland reports that such columns may be safely purged with a sodium hydroxide solution to clean unwanted, highly retained materials such as endotoxins from the column bed. Buffers made with lithium salts are less aggressive at high pH levels than those prepared with sodium salts.

Strongly basic compounds may be successfully separated with good column efficiency and shapes at pH levels in instances in which solutes are free bases. The scientists anticipate, though, that operation of silica-based columns at high pH levels will shorten column life, compared with much longer operation at lower pH levels. They are presently studying the stability of endcapped dimethyl-C_{18} columns at high pH level operating conditions to determine if the lifetime of silica-based columns can be extended using this approach. The Rockland Technologies work is detailed in the *Journal of Chromatographic Science* [**34**, 309-313].

Process that Purifies Hemoglobin

The development of hemoglobin based blood substitutes continues to command commercial attention. Recent developments have shown that hemoglobin from mammalian blood cells, after suitable modification such as intramolecular crosslinking and in some instances polymerization, has promise as the basis of a blood substitute. As development has proceeded, however, the requirements for purity of the hemoglobin have steadily increased. A chromatographic process for purifying hemoglobin (U.S. Patent 5,545,328) has been developed by researchers at Hemosol Inc. (Etobicoke, Canada).

At one time it was believed that hemoglobin simply needed to be stroma free, a condition achieved by washing and gentle lysing of the red blood cells, followed by filtration of the lysate. Subsequently, it was found that the presence of trace residues of impurities such as phospholipids led to more specific reactions, e.g. vasoconstriction, to the product in animal trials. Even after the product has been subjected to several diafiltration steps, it still contains unacceptably high traces of potentially harmful im-

purities such as erythrocyte enzymes, modified and variant forms of hemoglobin, phospholipids and surface antigens.

Chemical crosslinking of hemoglobin for the preparation of the basis of a blood substitute commonly produces a mixture of hemoglobin species. These must be subsequently be separated. Since they are, in many cases, almost identical in molecular weight and chemical composition, this separation presents difficulties.

Chromatographic methods have been applied to the purification of hemoglobin solutions. One such method applies the techniques of affinity chromatography to hemoglobin purification, using columns in which a ligand showing preferential chemical binding affinity to the DPG site of hemoglobin was bound to the stationary phase of the column. Ion exchange chromatographic techniques have also been used for hemoglobin purification. These approaches have not been attractive for large scale production, owing to the limitation of low loading capacities necessary to achieve sufficient resolution of the hemoglobin products.

Using the Hemosol method, a preselected hemoglobin species is separated from contaminants having a different acidity from that of the preselected hemoglobin species, by an overload displacement chromatography process. To remove more acidic contaminants, the process is conducted under anion exchange conditions. To remove more basic contaminants, the process is conducted under cation exchange conditions. In either case, the exchange column is overloaded to displace the hemoglobin species therefrom with contaminants having greater affinity for the column, and using the impure hemoglobin solution as the displacer.

Chromat fast Moves to Higher Sp ed

There is increased emphasis toward so called "high speed gas chromatography" or "high speed GC." Applications include process stream monitoring, environmental monitoring, and engine exhaust gas analysis. Ideally such systems would be able to perform an analysis within several seconds which previously took several minutes or more. Increasing the speed of analysis can be achieved by providing a relatively short separation column or by using other techniques for causing components of interest to traverse the column quickly.

Chromatofast, Inc. (912 N. Main St., Ann Arbor, MI 48104-1035; Tel: 313/662-3410) has found a way to increase the speed, operational flexibility, and accuracy of a gas chromatography system (U.S. Patent 5,547,497).

To provide useful information, the individual analyte components must elute separately at the detector, thus producing distinct peaks. As the length of time that the sample is injected at the inlet end of the column increases, the peaks produced by elution of the components tend to broaden.

A narrow sample "plug" must be presented at the column during injection in order to provide gas chromatography evaluation in a small period of time. It is for this reason that the dead volume associated with conventional cold trap type gas chromatography systems is a disadvantage.

Because during the collection mode of operation, the analyte condenses near the inlet end of the capillary tube (in terms of the direction of flow of carrier gas during injection), it is necessary to insure that region is sufficiently heated to vaporize all of the components of interest of the mixture during the injection step. This requirement leads to some portions of the cold trap sample tube being heated to a significantly higher temperature than is necessary to vaporize the sample collected at the inlet end of the sample tube. The analyte is exposed to the excessive temperatures for the length of time necessary to conduct them entirely through the focusing chamber.

In a reverse flow cold trapping apparatus, during the trapping mode of operation, the more volatile (lower boiling point) compounds have a tendency to completely traverse the cold trap before the less volatile (higher boiling point) compounds have entered the cold trap. The high rate of traversal of the low boiling point compounds makes it difficult to cryofocus (or cold trap) the lower boiling point and the higher boiling point compounds substantially simultaneously.

This movement of the low boiling point compounds generally results in a loss of lower boiling point compounds when attempting to cryofocus and perform detection on the higher boiling point compounds as well. Consequently, it would be extremely beneficial if it were possible to develop a cold trap apparatus which decreases the rate of traversal through the cold trap of the lower boiling point compounds so that the higher boiling point compounds may also be cryofocused substantially simultaneously.

Venom Research at Texas A&M

The Natural Toxins Institute at Texas A&M University—Kingsville uses the latest technology to study natural toxins from animals, plants and microorganisms. Their research focus is on the biochemistry of snake

toxins and animals that have a natural resistance to snake venoms.

The venom research program at Texas A&M University was among the first to show that certain warm-blooded animals have a natural resistance to snake venom. Snakes are venomous animals that use their venom for capturing, digesting prey, and creating medical emergencies when humans are envenomated. Certain warm-blooded animals have a natural resistance to snake venom.

Fast Performance Liquid Chromatography (FPLC) is being used at the Institute for the purification of hemorrhagins of *Crotalus atrox*, Western Diamondback rattlesnake, venom. FPLC is a type of liquid chromatography where the solvent velocity is controlled by pumps. The pumps control the constant flow rate of the solvents. The solvents are accessed through tubing from an outside reservoir. The flow rate of the solvent is set through computer input and controlled by pumps.

According to Pharmacia, maker of the FPLC system used at the Institute, the method is the most successful way to purify biomolecules. A combination of state-of-the-art separation media, instrumentation and software, FPLC is the industry standard for small scale purification, analysis and methods development.

Antihemorrhagins have been isolated and characterized from four different warm-blooded animals (Gray Woodrat, *Neotoma micropus*; Opossum, *Didelphis virginiana*; Mexican Ground Squirrel, *Spermophilus mexicanus*; and Hispid Cotton Rat, *Sigmodon hispidus*). The lab is interested in the mechanism by which naturally occurring antihemorrhagins neutralize hemorrhagic activity in snake venoms.

The antihemorrhagins isolated are not antibodies and do not form precipitates. The antihemorrhagins have molecular weights less than antibodies and an isoelectric pH (4.2) similar to albumin. They appear to neutralize all hemorrhagic activity in snake venoms tested. An extensive library of monoclonal antibodies has been developed to study snake venoms and antihemorrhagins found in resistant animals.

CONTROLLED RELEASE

Delivery System Prevents Neuron Loss

Huntington's disease, which affects more than 25,000 patients in the U.S., is a genetically determined, progressive neurodegenerative disease for which there is no known cure. The movement disorders that are symptomatic of the disease are caused by the death of specific neurons within the striatum of the brain. CytoTherapeutics, Inc. (2 Richmond Square, Providence, RI 02906; Tel: 401/272-3310, Fax: 401/272-3485) has reported that human ciliary neurotrophic factor, or hCNTF, delivered via CytoTherapeutics' encapsulated-cell devices, prevented the loss of specific neurons that would otherwise have died in a rodent model of Huntington's disease.

The results from the study, as reported by Dwaine F. Emerich, Ph.D., of CytoTherapeutics, and Jeffrey H. Kordower, Ph.D., of Rush-Presbyterian Medical Center in the current issue of the *Journal of Neuroscience* [**67**, 2, 1996], represent the first definitive *in vivo* demonstration that a growth factor can prevent the loss of the specific neuronal population affected in Huntington's disease. The hCNTF-producing devices also significantly reduced certain movement abnormalities in the animal model related to Huntington's disease.

Growth factors, alone and in combination, are believed to have great potential for halting the progressive loss of neuronal tissue characteristic of many central nervous system, or CNS, disorders. CytoTherapeutics is investigating the potential use of its encapsulated cell products to deliver additional growth factors to treat Huntington's disease. The company believes that its technology may represent a practical means of delivering long-term, stable quantities of such growth factors across the blood-brain barrier, avoiding many of the side effects associated with current methods for delivering these substances within the CNS.

Researchers utilized CytoTherapeutics' cell-containing devices to deliver hCNTF. Their model for Huntington's disease is based on the injection of quinolinic acid (QA) into the striatal region of the animals' brains to produce death of specific neurons similar to that found in Huntington's disease. Prior to the unilateral QA lesioning, CytoTherapeutics' devices were implanted into the brains of some of the animals. Animals implanted with hCNTF-secreting devices maintained most of the neuronal cells that would normally have been lost following the lesion. The researchers also reported the hCNTF-producing devices significantly reduced cer-

tain specific movement abnormalities that are characteristic of Huntington's disease in the lesioned animals.

The investigation into the delivery of hCNTF to treat Huntington's disease builds on a previous study conducted by Drs. Emerich and Kordower reported in 1994 in *Experimental Neurology*. That study employed the same rodent model for Huntington's disease, though the devices implanted into the brains of the rodents delivered human nerve growth factor, or hNGF.

Paralleling the results from the current study, the delivery of hNGF directly to the CNS of the rodents produced sparing of a specific neuronal population and a corresponding reduction in movement abnormalities associated with Huntington's disease. This study was the first to correlate the preservation of a specific population of neurons with the reduction of movement abnormalities in an animal model related to Huntington's disease.

Anxiety Patch Pact with Sano

Bristol-Myers Squibb Co. (345 Park Ave., New York, NY 10154-0004; Tel: 212/546-4000) and Sano Corp. (3250 Commerce Pkwy., Miramar, FL 33025; Tel: 954/430-3340) have struck a pact for Bristol-Myers to complete clinical testing and market Sano's transdermal formulations of Bristol-Myers' BuSpar, a prescription drug used to treat anxiety.

Terms state that Sano will receive payments from Bristol-Myers Squibb including an immediate payment of $15 million. The company will receive additional payments upon BuSpar reaching certain clinical and regulatory milestones. Provided all milestones are achieved, the premarketing value of the agreement is about $40 million.

Sano also will manufacture transdermal BuSpar for Bristol-Myers and receive a percentage of transdermal BuSpar net sales. BuSpar is an oral treatment for anxiety and is used in many countries as a three-times daily treatment. It was recently approved in the U.S. as a twice-daily treatment. Sano has developed transdermal patches of BuSpar, which are currently in Phase III clinical trials.

INDUSTRY NEWS

BioSepra Achieves Profitability

The achievement by BioSepra, Inc. (111 Locke Dr., Marlborough, MA 01752; Tel: 508/481-6802 or 800/752-5277, Fax: 508/480-8785) of its first quarter of profitability marks a milestone in the growth of the young biotechnology company. For the three months ended June 30, 1996, BioSepra recorded net revenues of $4.3 million and net income of $53,000, or $0.01 per share. The results compare with revenues of $3.7 million and a net loss of $6.6 million, or $0.94 per share, for the same quarter a year earlier. Product gross margins improved to 51% of current quarter sales, compared with 33% in the second quarter in 1995.

Investors haven't rewarded the performance, though. The company's stock (Nasdaq: BSEP) is trading in the 3.125 area (as of August 20, 1996), well off the 6.875 achieved during the third quarter of 1995 and the 7.750 reached in 1994. For the six months ended June 30, 196, BioSepra reported revenues of $7.1 million, and a net loss of $1.1 million, or $0.16 per share, compared with revenues of $6.6 million and a net loss of $9.7 million, or $1.39 per share, for the same period in 1995.

"As a public technology company, we are obligated to focus on growth and profitability," says Jean-Marie Vogel, president and CEO. "In this quarter, we continued to demonstrate this commitment. We have real growth in orders, sales, margins, and profitability." During the quarter, the company received larger than expected orders from its marketing partner, Beckman Instruments, Inc. for the jointly developed BioSys workstation. The company also extended its partnership to include a new marketing alliance for the Japanese market.

Sales of consumable trademarked HyperD media continued to increase, both to Beckman Instruments and to large biopharmaceutical companies. With more sales to companies involved in gene therapy, BioSepra is working toward leveraging the superior performance of HyperD in plasmids purification to position the company in the larger genomics market. Other key BioSepra product lines include its trademarked Rational Process Design software intended to facilitate process scaleup for various biomanufacturing processes and its trademarked ProSys workstation. The workstation is an advanced biochromatography system said to provide both computer aided bioprocess engineering capabilities and the automation of experimentation.

The system is intended to permit users to optimize process parameters based on a small number of experiments and simulated the performance of alternative designs in a commercial environment to determine resulting process characteristics, equipment requirements, and operating and

capital costs. The ProSys workstation is designed for use early in the product development cycle to create effective production methods and guide process design engineers toward an optimal process for all levels of production.

BioSepra has also introduced its trademarked Heparin HyperD affinity chromatography sorbent, said to provide high binding capacity at high flow rates. The advantages, says the company, stem from its trademarked HyperDiffusion technology, which provides very efficient mass transfer at high speed. The HyperDiffusion properties, evident in BioSepra's trademarked Q, S HyperD ion exchangers, were improved for a range of affinity chromatography sorbents. The rigid composite structure and proprietary hydrogel-filled pores provide affinity media with superior dynamic capacity for proteins over a full range of linear velocities up to 1,100 cm/hr. and more.

Heparin HyperD is perfectly dedicated to production processes, since the HyperD matrix is rigid and incompressible. No pressure or shrinkage can occur. The matrix, as well as the chemical link of the ligand, are particularly resistant and stable. Heparin HyperD can withstand solutions of sodium hydroxide for cleaning procedures.

BioSepra's has provided an update on its ongoing litigation with PerSeptive Biosystems, Inc. (500 Old Connecticut Path, Framingham, MA 01701; Tel: 508/383-7700, Fax: 508/383-7880). PerSeptive alleges that the production of HyperD chromatography media by BioSepra (and its major stockholder, Sepracor) infringes four PerSeptive patents. BioSepra has counterclaimed unfair competition by PerSeptive.

The U.S. District Court for the District of Massachusetts granted BioSepra's request for a summary judgment with respect to three of PerSeptive's trademarked Perfusion chromatography patents, ruling that parties other than those claimed by PerSeptive had been involved in developing the technology outlined in the Perfusion chromatography patents. Subsequently, the court denied PerSeptive's motion for immediate appeal. The effect of the two court rulings, says BioSepra, is that in order to correct inventorship, PerSeptive must bear the burden of proving that its initial designation of inventors was done without deceptive intent.

BioSepra's contention is that, if PerSeptive is able to correct inventorship, the presently unnamed inventors would have independent rights to license the technology outlined in the Perfusion patents. If inventorship cannot be corrected, the Perfusion patents would be ruled invalid, says BioSepra.

BioSepra says that it has expanded an strengthened its worldwide distribution network. In the important biopharmaceutical markets of Switzerland and Germany, as well as in Scandinavia and Ireland, the company appointed new distributors for its chromatography media and process development instrumentation.

PerSeptive Narrows the Gap

PerSeptive Biosystems, Inc. (500 Old Connecticut Path, Framingham, MA 01701; Tel: 508/383-7700, Fax: 508/383-7880) has reported total product revenue of $18.2 million for its third fiscal quarter ended June 30, 1996. Revenue for the comparable period during fiscal 1995 was comprised of $17.8 million of product revenue and $5 million of contract revenue derived from PTC-II, an independent research and development company which was acquired by PerSeptive in March 1996.

Starting with the third quarter of fiscal 1996, the company no longer receives PTC-II contract research revenues. The net loss for the third fiscal quarter of 1996 was $6.5 million. The net loss for the comparable period in fiscal 1995 was $16.2 million.

For the fiscal 9-month period ended June 30, 1996, product revenues were $56.6 million, as compared to $50.3 million for the same period in fiscal 1995, representing product revenue growth of 12.6%. The comparable 9-month period in fiscal 1995 included significant revenue that had been restated from fiscal 1994.

Noubar B. Afeyan, PerSeptive's CEO, said product sales for the third quarter increased in the company's Analysis business segment by 68% over last year. The order rate in its Purification business segment also grew substantially over last year. Afeyan says he expects the recent release of Vision and BioCAD 700E Workstations to result in increased marketshare. "Although product sales in our Synthesis business segment have declined during the past four quarters by about 20%, recent product introductions including PNA (Peptide Nucleic Acids), MOSS (Multiple Oligo Synthesizer) and Pioneer (Peptide Synthesizer), resulted in revenue growth in the third quarter over the prior quarter."

Jack Smith, PerSeptive's president added that total expenses were down from $17.1 to $14.3 million when comparing the second and third quarter of fiscal 1996, in line with expectations following the PTC-II acquisition. "With the increasing market pen-

etration of our products, PerSeptive is playing a leading role in transforming biomedical research and drug development making them more automated, much faster and more economical. Now, we must also transform PerSeptive in order to achieve our goal of sustained profitability in the near future," Smith explained.

Isco Buys Suprex

Isco, Inc. (P.O. Box 5347, Lincoln, NE 68505; Tel: 402/464-0231, Fax: 402/464-0318) announced that it has signed an agreement to acquire the assets of privately held Suprex Corp. (125 William Pitt Way, Pittsburgh, PA 15238; Tel: 412/826-5200). The transaction has been approved by each company's Board of Directors. Subject to approval by the shareholders of Suprex, it is the intent of both parties to close the transaction within 10 days. Additional terms and conditions of the agreement were not disclosed.

Doug Grant, president and COO of Isco, said the company believes the acquisition will enhance Isco's long-term growth objectives. "We expect that Suprex products will make an immediate and positive contribution to both sales and profitability."

Like Isco, Suprex designs manufactures, and markets supercritical fluid extraction (SFE) instruments for sample preparation in research and process support labs. Key market segments served include food processing, plastics and polymers, and environmental analysis.

Grant added that both Suprex and Isco have made significant product development investments, and the combined product lines and customer bases now provide enhanced growth opportunities. "Going forward, our priority is to strengthen our marketing, sales, and applications capabilities." Acquiring Suprex allows Isco to achieve a market share in excess of 50%, capitalize on a significant engineering investment, and quickly create a strong and customer oriented sales and marketing organization for SFE products.

High-Tech Separations Stock Watch
(At Close, September 3, 1996)

Company	Symbol	Current Price	Last Month	Change
Advanced Magnetics	AVM	18.750	18.000	+0.750
Ametek, Inc.	AME	19.500	18.500	+1.000
Beckman Instruments	BEC	37.000	36.875	+0.125
Bio-Rad Laboratories	BIO/A	28.125	29.250	-1.125
Biosepra	BSEP	3.625	3.000	+0.625
Celgene	CELG	8.500	8.000	+0.500
Cytotherapeutics	CTII	10.875	8.125	+2.750
Dionex	DNEX	36.875	34.750	+2.125
Hewlett-Packard	HWP	44.250	43.750	+0.500
Isco, Inc.	ISKO	10.125	9.500	+0.625
Olin Corp.	OLN	78.875	85.000	-6.125
Osmonics	OSM	19.250	20.750	-1.500
Perkin Elmer Corp.	PKN	51.875	51.500	+0.375
PerSeptive Biosystems	PBIO	6.875	7.750	-0.875
Sepracor	SEPR	12.750	13.875	-1.125
Varian Associates	VAR	45.750	44.750	+1.000

Advanced Magnetics Looks to the East

Advanced Magnetics, Inc. (61 Mooney St., Cambridge, MA 02138; Tel: 617/497-2070, Fax: 617/547-2445) has signed an agreement with TaeJoon Pharmaceutical Co., Ltd. for the exclusive distribution in South Korea of Feridex I.V., the company's contrast agent for magnetic resonance imaging (MRI) of liver lesions.

Jerome Goldstein, president and CEO of Advanced Magnetics, said the agreement is an important step forward in establishing his company as a global player in the development of contrast agents for use with magnetic resonance imaging. "South Korea is developing into a significant MRI contrast agent market and we look forward to working with TaeJoon to ensure the successful launch of Feridex I.V.," Goldstein added. Advanced Magnetics also has distribution agreements in place for Feridex I.V. in the U.S., Japan, Europe and Brazil.

Under the agreement, TaeJoon Pharmaceutical has the responsibility to obtain and maintain South Korean government registration and permission to sell Feridex I.V.

Celgene Reports a Net Loss

Celgene Corp. (7 Powderhorn Dr., Warren, NJ 07054; Tel: 908/271-1001, Fax: 908/271-4184) reported a net loss for the second quarter of $3.808 million, compared to $2.257 million a year ago. The quarter, which ended

June 30th also marked a significant increase in revenues to $1.166 million, as compared with $404,000 in the same quarter in 1995, and $819,000 in the first quarter of 1996.

Total revenues for the first six months of 1996 were $1.985 million, approximately triple the volume from the same period last year. The increase in revenues primarily reflects expanded sales of chirally pure chemical intermediates, which reached record levels for the second quarter and first half. The net loss for six months was $6.842 million, compared with $4.404 million for the 1995 period. The increase in operating losses are primarily the result of expanded research and development efforts, and clinical trial costs in immunotherapeutics.

The company's cash and marketable securities totaled $28.1 million at the end of June compared with $11.7 million at year end 1995. The increase reflects $23.8 million in net proceeds from a private placement of convertible preferred stock in March 1996. As of June 30, 1996, shareholders' equity stood at $27.037 million, up from $7.142 million at the close of the 1995 fiscal year. Weighted average number of shares outstanding was 9,079,000.

Millipore Cashes in

PerSeptive Biosystems, Inc. (500 Old Connecticut Path, Framingham, MA 01701; Tel: 508/383-7700, Fax: 508/383-7880) has issued 1,248,050 shares of its registered Common Stock to Millipore Corp. (80 Ashby Rd., Bedford, MA 01730; Tel: 617/275-9200, Fax: 617/275-5550) in payment of the second $10 million installment due upon the redemption by Millipore of 1,000 shares of the PerSeptive's non-voting Redeemable Preferred Stock. The Redeemable Preferred Stock was issued to Millipore in connection with the acquisition by PerSeptive of Millipore's BioSearch division in August 1994.

PerSeptive Biosystems develops, manufactures and markets an integrated line of proprietary consumable products and advanced instrumentation systems for the purification, analysis and synthesis of biomolecules. PerSeptive's product lines are based on its patented core technologies in the fields of chromatography, immunoassay, solid-phase synthesis, rational surface design, biological mass spectrometry and magnetic separations.

MOLECULAR SIEVES

Composite Enhances Solid Phase Extraction

Solid phase extraction (SPE) has received considerable attention because of environmental concerns. SPE is used for pre-concentration and cleanup of analytical samples, purification of various chemicals, and removal of toxic or valuable substances from aqueous substances

The use of siliceous molecular sieves as components in microporous membranes in separation science is known but not fully explored. Donald Hagen, Paul Hansen, and Craig Markell of 3M (3M Center, St. Paul, MN 55144-1000; Tel: 612/733-1110) have been exploring entrapping a small-diameter (at most 3-5 micrometers) molecular sieve into a 3M Empore-brand polytetrafluoroethylene membrane or into an MS particle loaded BMF membrane.

Flexible membrane composites greatly enhance SPE mechanisms, particularly column- or cartridge-type SPE due to faster flow through rates and lower pressure drop. The membranes also have utility in thin layer chromatography and other planar chromatography applications. They show particular selectivity in sorbing certain classes of organic molecules, such as large hydrophobic molecules (e.g., larger than hexane), and small polar molecules (e.g., 2-4 carbon atoms, such as ethanol, propanol, butanol, methyl ethyl ketone, and ethyl acetate) out of water. Multiple analytes can be removed simultaneously.

The 3M composites, which are protected by U.S. Patent 5,529,686, are used as either a membrane or a flat sheet material with very favorable diffusion kinetics for sorptive and reactive interactions. They consist of a porous nonwoven matrix of polytetrafluoroethylene (PTFE) fibrils and melt-blown microfibers (BMF). Enmeshed within the matrix are sorptive or reactive hydrophobic siliceous molecular sieve particulates, with the ratio of molecular sieves to matrix ranging from 40:1 to 1:40 (preferably 19:1 to 1:4). The enmeshed particulates comprise 35-100% by weight percent of molecular sieves.

All of the 3-D channel, siliceous molecular sieves used have pore diameters of about 0.6 nanometers (or 6 angstroms) in diameter. The crystalline molecular sieves (either functionalized or carbon-modified) may be in any suitable form, with powders or

aggregates being preferred. The aggregates may be any convenient shape (e.g., spheres, cylinders, free form, etc.). Binders, such as silica or alumina, may be used when forming the aggregates. The molecular sieves chosen can display unique reversed, normal phase, and ion exchange behavior in addition to molecular sieve properties.

Degussa Method Has Universal Appeal

Degussa Aktiengesellschaft (Frankfurt, Germany) can now modify molecular sieves with solid state ion exchange (U.S. Patent 5,545,784). The molecular sieves ("mol sieves") are modified by an ion exchange process where metal cations are introduced into the molecular sieves by means of solid state ion exchange.

The solid state ion exchange can be carried out as follows: a weighed amount of calcined and activated zeolite is intimately mixed with a precalculated amount of $PtCl_2$, $PdCl_2$, $RhCl_3$, $CuCl_2$, V_2O_5 or another compound of the noble metals (e.g., corresponding halides or oxides). The solids mixture is then heated in a current of inert gas (e.g., a current of helium gas or of nitrogen) to temperatures of 400°-600°C, then cooled down to room temperature and subsequently reduced in a current of hydrogen for 10-14 hrs. at 280°-350°C in order to produce small metal clusters from the cationically introduced metal. The resulting mol sieves are used for hydrogenating olefinic compounds to form alkanes.

A method was previously developed for introducing noble metals such as platinum or palladium into medium-pored and wide-pored zeolites by way of ion exchange in aqueous suspension with the appropriate tetraamine complexes. This method yields a high distribution of the noble metal in the crystallite interior of wide-pored zeolites and medium-pored zeolites.

Small-pored zeolites cannot be doped in this manner with platinum or palladium because the noble-metal complex is too bulky to be able to diffuse into the eight-membered ring channels of these zeolites. The only known method for introducing noble metals into the interstices of small-pored zeolites, prior to the Degussa development, was to add the noble-metal complex in the desired amount to the synthesis gel for the zeolite production prior to crystallization so that the zeolite crystallizes around the complex. A shape-selective hydrogenation catalyst can be produced by introducing $Pt(NH_3)_4Cl_2$ into the synthesis gel.

SUPERCRITICAL EXTRACTION

PNNL Aggregates Boost Performance

A decade of research at Pacific Northwest National Lab (PNNL, P.O. Box 999, Richland, WA 99352) allows the group to offer various types of molecular aggregates to significantly boost the performance of supercritical fluids in reactions and separations. These molecular technologies were either invented at PNNL or largely developed here.

Reverse micelle and microemulsions comprise ultra-small (5-10 nm) droplets of water that are dispersed in the supercritical fluid solution by a surfactant. These systems are useful interactions, polymerization, and extractions including cleansing applications, metal chelates and ligands. We have available various ligands that will complex a range of metal ions and thereby dissolve them in a supercritical fluid such as supercritical carbon dioxide. Such systems are useful in metal-catalyzed homogeneous reactions and extractions of metal contaminates from waste.

In a major commitment to technology transfer from the laboratory to industry, the Supercritical Fluids Group at PNNL, which includes Clement Yonker, Lawrence Bowman, and John Fulton, maintains facilities for the development and evaluation of supercritical fluid processing. The microemulsion technology and the RESS (rapid expansion of supercritical fluid solutions) were first demonstrated at PNNL; Battelle, which operates PNNL, holds key patents in these areas. The research group has a wide range of spectroscopic techniques that are available for study of chemistry, physical chemistry, and separations in a road range of fluids from carbon dioxide to supercritical water.

Over the last three years, PNNL has been exploring the use of carbon dioxide as a replacement solvent for water in textile processing. The studies have demonstrated that carbon dioxide can be successfully used in dyeing, applying UV stabilizer and for the application and removal of "size." Large savings in energy and reductions in waste generated can be realized by switching to the "green" solvent.

Dynamic Extraction of Cedrelone

South African researchers have applied dynamic supercritical fluid extraction to obtain the limonoid compound cedrelone from wood of *Cedrela toona*, a South African tree of the family

Meliaceae, which includes mahogany.

William K. Modey, Dulcie A. Mulholland, and Mark W. Raynor (Dept. of Chemistry, University of Natal, King George V Ave., Durban 4001, South Africa) note that limonoids are a class of aromatic compounds obtained from plants of the families Meliaceae, Cneoraceae, and Rutaceae. Although not actively insecticidal, limonoids discourage grazing by insects and some are active against certain cancers.

The authors investigated supercritical fluid extraction as an alternative to time-consuming Soxhlet extraction. They found that SFE rarely achieves complete extraction from some matrices because some solute remains in the structure of a matrix and is only extracted with time. Raynor reports that they developed a kinetic extraction model which extrapolates data from short extractions to estimate the amount of cedrelone in ground wood.

Seasoned Cedrela wood was ground into 250-700 micron particles and dynamic extractions were performed. They also performed SFE extractions with 0.4 mol% methanol-modified CO_2 at 400 atm and 40°C for 40 min., and Soxhlet extractions with liquid hexane. The extracts were analyzed by capillary gas chromatography with flame ionization detection. Two major compounds in Cedrela extract were identified: cedrelone and geranyl geraniol. Cedrelone was the model compound for their extraction model.

After extrapolating total cedrelone by successive extractions at 300°for three samples, the authors performed extractions at 350°C for different lengths of time and plotted percentage yield against time. Raynor reports in *Journal of Chromatographic Science* [**34**-7, 320-325, 1996] that the results show a tailing-off of recovery with time and that 66% of total cedrelone is recovered in 8 min.

CALENDAR

October 17-19, 1996, The 52nd ACS Southwest Regional Meeting will be held in Houston. Contact: J.W. Hightower, Dept. of Chemical Engineering, 6100 S. Main St., M/S 362, Rice U, Houston, TX 77005-1892; Tel: 713/285-5906, email: reglmtgs@acs.org.

October 20-25, 1996, Recovery of Biological Products VIII will be held in Tucson, AZ. Contact: ACS Meetings Dept., 1155—16th St. NW, Washington, DC 20036; Tel: 202/872-6286, Fax: 202/872-6128, email: miscmtgs@acs.org.

October 27-30, 1996, The 1996 Fourteenth Annual Membrane Technology Planning Conference will be held in Newton, MA. For more information, contact: Business Communications Co., Inc., 23 Van Zant, No. 13, Norwalk, CT 06855; Tel: 203/853-4266, Fax: 203/853-0348.